

TITLE OF THE INVENTION
ANTIMICROBIAL WOUND COVERING ARTICLE

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P24007.S03

ANTIMICROBIAL WOUND COVERING ARTICLE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority under 35 U.S.C. §119 of German Patent Application No. 103 16 156.2, filed on April 9, 2003, the disclosure of which is expressly incorporated by reference herein in its entirety.

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0002] The present invention relates to an antimicrobial wound covering article. In particular, the invention relates to an antimicrobial wound covering article which comprises a polyurethane resin in combination with a particulate, silver containing glass, which glass is capable of releasing silver ions when coming into contact with a wound exudate.

2. Discussion of Background Information

[0003] The treatment and healing of bacterially contaminated and/or infected skin and wounds is a great challenge to medicine and the natural sciences. Poorly healing wounds and chronic wounds in particular are often populated by a wide variety of microorganisms which greatly delay or sometimes even prevent entirely the course of healing. Even with acute wounds, however, caused by trauma, surgical intervention, or even just simple injury, the penetration of pathogenic microorganisms cannot be ruled out in every case.

[0004] As a result of the penetration of germs, the wound is colonized with microorganisms. A wound populated with more than 10^5 CFU/g is referred to as an infected wound (M. C. Robson "Clinical Research can improve the outcome of treatment of problem wounds: Infection as a Paradigm", 8th Annual Meeting of the ETRS, Copenhagen, DK, August 27-30, 1998). The massive colonization of the wound medium with microorganisms may result in a massive interference with the course of healing, which may lead ultimately to mortality. Frequent causative organisms of bacterial wound infections belong to the genera *Pseudomonas*, *Staphylococcus*, *Clostridium* and, among the yeasts and molds, to the genera *Candida* and *Aspergillus*. Limitation to a few species

is impossible, since many of the microorganisms may be regarded as opportunistic pathogens.

[0005] Various possibilities are described for removing microorganisms from the contaminated or infected tissue of a wound and/or for killing them therein. In addition to the oral administration of antibiotics, the removal of pathogenic microorganisms from a wound may be achieved, in accordance with the prior art, by the topical application of a disinfectant or an antibiotic. However, antiseptics and antibiotics are cytotoxic, and, moreover, many pathogenic strains have developed resistances to antibiotics. The fact that the development of resistance even to an antiseptic is possible has been reported for triclosan-resistant *E. coli* bacteria (McMurry, L. M. et al., FEMS Microbiol Lett. 1998, 166(2): 305-9, Cookson, B. D. et al., Lancet 1991, 337 (8756): 1548-9; Uhl, S., Lancet 1993, 342(8865): 248). The principal critical factor in that case was the widespread and prophylactic use of triclosan (Irgasan®) in soaps, deodorants, textiles and plastics.

[0006] A well-known use, for example, for the antimicrobial and/or preventive therapy of contaminated or infected wounds is that of oxidants (for example iodine tincture) or antiseptics (for example, ointments containing silver sulfadiazine). Another form in which such agents are used is that of correspondingly antimicrobially coated or impregnated wound coverings and dressing materials. The use of zeolites containing silver is also known in the field of wound management products. DE-A1-19958458 provides an overview of the known antimicrobially active dressing materials containing silver. DE-A1-19958458 discloses wound coverings which comprise a synthetic polymer material that contains zeolites having metal ions therein. Also known, from EP-A1-1116698 and EP-A1-1116700, are silver containing glasses that show antimicrobial activity. However, these are embedded in thermoplastic polymers that are used only in the household and sanitary sectors in a variety of forms, such as wallpaper, cutting boards, and the like.

[0007] The development of antimicrobial wound dressings focuses not only on antimicrobial activity, but also on the creation of a moist wound environment, which – in contrast to dry wound treatment such as, e.g., with gauze compresses – provides physiological, and hence better, conditions for the natural processes of wound healing.

[0008] EP-A1-1159972 discloses a wound dressing consisting of a self-adhesive hydrocolloid composition that permits a moist wound environment and contains an antimicrobial agent which comprises silver, copper, and zinc.

[0009] An antibacterial hydrocolloid dressing is available on the market from Coloplast company under the trade name Contreet-H®. Due to an impregnation with ionic silver, this dressing permits moist wound treatment and antibacterial activity. Corresponding dressings are described in WO 00/09173 and U.S. Patent No. 5,681,575, as well as in WO 02/062403 and WO 02/078755. WO 02/062403 describes an antimicrobial wound dressing that contains, in an adhesive matrix, a silver containing complex which comprises at least one element of Group IV of the Periodic Table of Elements. Titanium, hafnium and zirconium are mentioned as preferred elements, and the complex preferably is a phosphate complex. The silver ions, present in an amount of 0.01 to 30 mg/cm² of wound dressing, are released only on contact with an ionic solution. In this context, only adhesive materials that do not reduce the release of the silver or the antimicrobial activity of the silver are suitable. As an example, a polyurethane foam is described as a matrix, wherein the employment of a foam is a critical factor with respect to the release rate.

[0010] WO 02/078755 describes an antimicrobial wound dressing showing a release of silver of from 50 to 10,000 µg/cm² and an absorption capacity for wound exudate of more than 0.09 g/cm². Like in the case of WO 02/062403, the silver compounds are present in the form of complexes with elements of Group IV of the Periodic Table. A zirconium phosphate complex is preferred here as well. The very wide range of release rates specified in WO 02/078755 encompasses release rates that are also achieved with the silver containing antimicrobial wound dressings of the prior art.

[0011] The entire disclosures of the documents discussed above, as well as those of all other documents mentioned in the present specification, are expressly incorporated by reference herein as if the disclosure of each of these documents in its entirety were part of the present specification.

[0012] All of the above-described known antimicrobial wound dressings which contain silver have at least one problem in common, however. They all exhibit dark discoloration after a certain period due to the formation of elemental silver or silver oxide. This dark discoloration is accelerated by heat, moisture, light and/or the influence of radiation.

Moreover, the unappealing dark brown or black silver oxide no longer has any germicidal effect, with the result that the efficacy of the known dressing materials suffers with regard to durability. The antimicrobial effect diminishes after a short time unless expensive sealing and packaging is employed for such products. In particular, these products do not satisfy the aesthetic demands of consumers.

[0013] It would be advantageous to have available an antimicrobial polymer material which, when used as a dressing material, especially as a wound covering, combines all of the desirable characteristics of the known individual antimicrobial dressing materials while at the same time avoiding the disadvantages of these materials.

[0014] In particular, the polymer material desirably should satisfy all or most of the following requirements:

- preferably be self-adhesive to obviate the need for additional attachment materials,
- have a simple structure so that it can easily be handled even by laypeople,
- generate a moist wound environment where desirable,
- show antimicrobial activity, yet with a minimum content of active substance,
- store well without sacrificing any of the aforementioned properties,
- satisfy the aesthetic demands of consumers,
- be stable under external influences such as light, moisture and/or radiation and, in particular, show no discoloration even after having been exposed to these external influences for a relatively long time.

SUMMARY OF THE INVENTION

[0015] The present invention provides an antimicrobial wound covering article, wherein at least a part of the article comprises a polyurethane resin which is associated with a particulate, silver containing glass. When coming into contact with a wound exudate, the glass is capable of releasing silver ions.

[0016] In one aspect of the article, at least a part of the polyurethane resin may form a matrix which comprises at least a part of the particulate glass.

[0017] In another aspect of the article, at least a part of the particulate glass may be present on a surface of a structure which comprises the polyurethane resin.

[0018] In yet another aspect, at least a part of the polyurethane resin may form a sheet-like structure. For example, at least a part of the polyurethane resin and at least a part of the particulate glass may form a layer which has an area weight of from about 400 g/m² to about 1200 g/m² and/or has a thickness of from about 0.1 mm to about 2 mm, e.g., from about 0.4 mm to about 1.5 mm, or from about 0.6 mm to about 1.2 mm. Also, at least a part of the polyurethane resin and at least a part of the particulate glass may form a layer which has water vapor permeability of from about 100 g/(m²*24h) to about 5,000 g/(m²*24h), e.g., from about 250 g/(m²*24h) to about 2,500 g/(m²*24h), or from about 300 g/(m²*24h) to about 1,500 g/(m²*24h).

[0019] In a still further aspect, at least a part of the polyurethane resin may comprise a polyurethane foam. Alternatively or additionally, at least a part of the polyurethane resin may not be foamed.

[0020] In another aspect of the article, the polyurethane resin may form a gel-like material.

[0021] In another aspect, at least a part of an external surface of the article comprises the polyurethane resin.

[0022] In yet another aspect of the article, the polyurethane resin may have a liquid absorption capacity of from about 0.5 g/g to about 10 g/g, e.g., from about 1 g/g to about 6 g/g, or even from about 1.5 g/g to about 3.5 g/g.

[0023] In a still further aspect of the article, the polyurethane resin may be self-adhesive.

[0024] In yet another aspect of the article, the polyurethane resin may comprise a pigment, for example, TiO₂, which may be present in an amount of from about 0.01 % by weight to about 2 % by weight, based on the weight of the polyurethane resin.

[0025] In a still further aspect of the article, the article may further comprise a superabsorber, for example, in an amount of from about 0.5 % by weight to about 30 % by weight, based on the weight of the polyurethane.

[0026] In another aspect, the polyurethane may comprise units which are derived from a polyol component which comprises at least one polyether polyol, e.g., a polyether

polyol which comprises from about 2 to about 6 hydroxy groups and/or has a hydroxy number of from about 20 to about 120 and/or comprises at least about 10 % by weight of units which are derived from ethylene oxide. By way of non-limiting example, the at least one polyether polyol may comprise units which are derived from ethylene oxide, propylene oxide and at least one compound having more than two hydroxy groups such as, e.g., pentaerythritol. The at least one polyether polyol may, for example, have a weight average molecular weight of from about 2,000 to about 8,000.

[0027] In a still further aspect, the polyurethane may comprise units which are derived from a polyisocyanate component which comprises at least one aliphatic polyisocyanate, for example, an aliphatic polyisocyanate which comprises at least one polymethylene diisocyanate having from about 2 to about 8 methylene groups such as, e.g., hexamethylene diisocyanate.

[0028] In another aspect of the article, the polyurethane may comprise units which are derived from at least one polyether polyol and at least one aliphatic diisocyanate, wherein these reactants may be those which have been discussed above.

[0029] In yet another aspect, the ratio of the number of free isocyanate groups in the polyisocyanate starting material to the number of free hydroxy groups in the polyol starting material for producing the polyurethane may be in the range of from about 0.3 to about 0.7. Alternatively or additionally, the product of the functionality of the polyisocyanate starting material and the functionality of the polyol starting material for producing the polyurethane may be at least about 5.2. Furthermore, the polyurethane resin of the article according to the present invention may comprise the residue of a Bi containing catalyst.

[0030] In another aspect, the polyurethane resin may have been formed by reacting at least one polyol and at least one polyisocyanate in the presence of the particulate glass.

[0031] In a still further aspect of the article, the glass may comprise particles having a volume-related particle size of from about 0.1 μm to about 10 μm and/or glass fibers. In another aspect, the glass preferably comprises not more than about 5 % by weight of residual water.

[0032] In another aspect, the glass preferably comprises about 40-60 mole-% of P_2O_5 , about 35-55 mole-% of at least one of CaO , MgO , ZnO and CuO , up to about 5 mole-%

of at least one of Na_2O , K_2O and Li_2O , and about 5-20 mole-% of at least one of SiO_2 , Al_2O_3 and B_2O_3 , and contains from about 0.1 % by weight to about 8 % by weight of Ag_2O . For example, the glass may comprises about 45-55 mole-% of P_2O_5 , about 40-50 mole-% of at least one of CaO and MgO , up to about 5 mole-% of at least one of Na_2O and K_2O , and about 5-10 mole-% of at least one of SiO_2 and Al_2O_3 , and may contain from about 0.5 % by weight to about 5 % by weight of Ag_2O , or the glass may comprise about 45-55 mole-% of P_2O_5 , about 40-50 mole-% of MgO , and about 5-10 mole-% of at least one of SiO_2 and Al_2O_3 , and may contain from about 1% by weight to about 3 % by weight of Ag_2O . Even more preferred is a glass which comprises about 49-51 mole-% of P_2O_5 , about 43-45 mole-% of MgO , and about 5-7 mole-% of Al_2O_3 , and contains from about 1.5 % by weight to about 2.5 % by weight of Ag_2O . It also is preferred for the glass to contain 0.5 to about 2.5 % by weight of Ag_2O .

[0033] In another aspect of the article of the present invention, the glass may be present in an amount of from about 0.01 % by weight to about 40 % by weight, preferably in an amount of from about 0.05 % by weight to about 10 % by weight, e.g., in an amount of from about 0.1 % by weight to about 5 % by weight, based on the combined weight of the glass and the polyurethane resin.

[0034] In a still further aspect, the article is capable of releasing silver ions for at least about 10 hours, preferably at least about 24 hours, when in contact with a wound exudate.

[0035] In another aspect of the article, the polyurethane resin may comprise at least one of elemental Al, Zn, Mg and basic compounds thereof, preferably in an amount of from about 0.01 % by weight to about 5 % by weight, based on the weight of the polyurethane resin.

[0036] In yet another aspect, the article may further comprise a backing material. The backing material may comprise a polyurethane. For example, the backing material may comprise a polyurethane sheet having a pressure sensitive adhesive on a side thereof which faces the polyurethane resin that is associated with the particulate glass. The polyurethane sheet may be substantially transparent.

[0037] In yet another aspect, the article of the present invention may be a bandage a wound dressing, a wound pad, or a compress.

[0038] In a still further aspect, the article preferably releases silver at a rate of from about 5 mg/(m²*24h) to about 50 mg/(m²*24h), e.g., from about 10 mg/(m²*24h) to about 40 mg/(m²*24h).

[0039] The present invention also provides a method of covering a wound, wherein the method comprises placing on the wound at least a portion of a wound covering article of the present invention, including the various aspects thereof, as discussed above.

[0040] In one aspect of the method, the polyurethane resin preferably is brought into direct contact with the wound.

[0041] The present invention further provides a process for making an antimicrobial wound covering article. The process comprises combining a silver containing, particulate glass and a polyurethane resin so that a mixture wherein the polyurethane resin is in direct contact with the particulate glass is formed.

[0042] In one preferred aspect of the process, the combining of the polyurethane resin and the glass comprises conducting, in the presence of the glass, a reaction between a polyol component and a polyisocyanate component to form the polyurethane. In another aspect, the process may further comprise shaping the mixture and affixing the shaped mixture to a backing layer. For example, the mixture may be bonded to the backing material through an adhesive. the backing material may comprise a polyurethane sheet.

[0043] In yet another aspect of the process, at least a part of the polyurethane resin and at least a part of the particulate glass are made into a sheet-like layer having a thickness of from about 0.1 mm to about 2 mm.

[0044] In a still further aspect of the process, the process may further comprise a sterilization of the article, for example, a sterilization which comprises irradiating the article with γ -rays. Preferably, the sterilization does not result in a noticeable discoloration of the article.

[0045] The article according to the present invention has antimicrobial properties and comprises a (substantially biocompatible) polyurethane resin. This polyurethane resin, may comprise a mixture of two or more different polyurethane polymers. These polymers may differ, by way of non-limiting example, in the nature of the units constituting the polyurethane (e.g., polyol and polyisocyanate starting materials), and the nature and relative amount of the starter compounds (e.g., polyhydric compounds having 2 or more

hydroxy groups and/or polyamines and/or other compounds having active hydrogen atoms) employed for the synthesis thereof. Moreover, the article may further comprise one or more substantially biocompatible non-polyurethane resins in addition to the polyurethane resin, although preferably in an amount of not more than about 50 % by weight, more preferably, not more than about 30 % by weight, e.g., not more than about 10 % by weight, based on the total amount of resin materials present. Non-limiting example of such additional resins are polymeric superabsorbers, mentioned above, as well as materials commonly used in wound healing, such as synthetic polymer materials, for example, polyacrylates, SIBS (styrene-isobutylene-styrene) block copolymers, SEBS (styrene-ethylene butylene-styrene) block copolymers, natural rubbers and also chitosans, alginates, hydrogels, hydrocolloids and the like.

[0046] It is noted that the term "polyurethane resin" as used in the present specification and in the appended claims, means a polyurethane resin composition which is obtained by combining polyurethane forming reactants (usually including at least one polyol and at least one polyisocyanate) in the presence of conventional additives such as, e.g., catalysts, antioxidants and other stabilizers, etc. In comparison thereto, the term "polyurethane" is used herein when the chemical entity as such, e.g., as representable by a structural formula, is referred to.

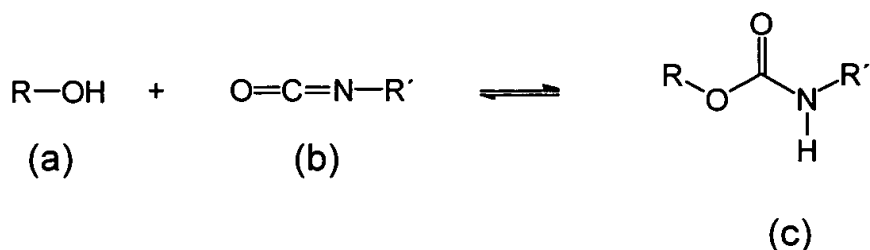
[0047] It is not absolutely necessary for the polyurethane resin to be foamed, as is required in the prior art for effective release of the silver. However, if desired, at least a part of the polyurethane resin may be foamed to provide the advantages discussed below.

[0048] Preferably, self-adhesive polyurethane resins are chosen in order to avoid the need for additional adhesive on the edge of the article of the present invention. Particularly preferred according to the present invention is the use of self-adhesive polyurethane resins that may be used as a hydroactive wound covering for moist wound healing. By way of non-limiting example, elastic, cross-linked polyurethanes as described, for example, in WO 97/43328 A1 may be used for this purpose. An area weight of a corresponding polyurethane structure may be, for example, in the range of from about 50 g/m² to about 2,500 g/m².

[0049] Generally, polyurethanes are prepared from the known starting materials of polyurethane chemistry according to known methods. Examples of such methods are

described, for example, in the following documents: DE-OS 3103499, DE-OS 3103500, EP 0 147 588 A1, EP 0 665 856 B1 and DE 196 18 825 A1.

[0050] A conventional process for synthesizing a polyurethane (c) is the reaction of an alcohol (a) with an isocyanate (b), as illustrated in the following reaction scheme:



[0051] A particular advantage of many polyurethane polymers or gels is their self-adhesive properties, which obviates the need for additional application of an adhesive layer to the polymeric material to affix the latter to the skin. For example, a polyurethane matrix which contains the silver containing glass may be sandwiched between a cover layer that is firmly anchored thereto, also known as the backing layer, and a removable release layer. The removable release layer serves to secure the adhesive layer on the backing layer, to improve transport and storage stability, and is removed before application to the skin.

[0052] Non-limiting examples of suitable polyurethanes for use in a matrix as discussed above are described in, e.g., DE 196 18 825, which document discloses hydrophilic, self-adhesive polyurethane gels which are made by using

- (a) polyether polyols having about 2 to about 6 hydroxyl groups, OH numbers of from about 20 to about 112, and an ethylene oxide (EO) content of $\geq 10\%$ by weight,
- (b) antioxidants,
- (c) bismuth(III) carboxylates based on carboxylic acids having about 2 to about 18 carbon atoms as polymerization catalysts, which carboxylates are soluble in the polyols (a), and
- (d) hexamethylene diisocyanate.

[0053] In these polyurethanes, the product of the functionalities of the polyurethane-forming components (a) and (d) is at least about 5.2, the amount of catalyst (c) ranges

from about 0.005 to about 0.25 % by weight based on the polyol (a), the amount of antioxidant (b) is in the range of from about 0.1 to about 1.0% by weight based on polyol (a). Furthermore, the ratio of the free NCO groups of component (d) and the free OH groups of component (a) (isocyanate index) is in the range of from about 0.30 to about 0.70.

[0054] When polyether polyols are employed as polyol components for the preparation of polyurethanes suitable for use in the present invention, those having 3 to 4, more preferably 4, hydroxyl groups, and an OH number of from about 20 to about 112, more preferably, of from about 30 to about 56, are preferably used. The ethylene oxide content of the polyether polyols preferably is \geq about 20 % by weight.

[0055] Polyether polyols for use in the preparation of polyurethanes are known per se and may be prepared, for example, by polymerizing epoxides such as, e.g., ethylene oxide, propylene oxide, butylene oxide or tetrahydrofuran, with themselves, or by subjecting these epoxides, preferably ethylene oxide and propylene oxide, optionally as a mixture with one another or separately in succession, to an addition reaction with starter components containing at least two reactive hydrogen atoms such as, e.g., water, ethylene glycol, propylene glycol, diethylene glycol, dipropylene glycol, glycerol, trimethylol propane, pentaerythritol, sorbitol and sucrose. Further examples of polyhydroxy compounds which may be used are disclosed, for example, in High Polymers, Vol. XVI, "Polyurethanes, Chemistry and Technology" (Saunders-Frisch, Interscience Publishers, New York, Vol. 1, 1962, pp. 32-42).

[0056] Preferred examples of polyisocyanates for the synthesis of polyurethanes for use in the present invention include monomeric and/or trimerized hexamethylene diisocyanate, and hexamethylene diisocyanate which may be modified by biuret, uretdione or allophanate groups, and/or may be prepolymerized with polyether polyols or mixtures of polyether polyols. These polyether polyols, in turn, are preferably based on the conventional starter compounds which contain 2 or more reactive hydrogen atoms and the conventional epoxides, such as ethylene oxide or propylene oxide, e.g, those having an OH number of ≤ 850 , preferably of from about 100 to about 600. Particularly preferred is the use of modified hexamethylene diisocyanate, in particular, hexamethylene diisocyanate modified by prepolymerization with polyether diols having

an OH number of from about 200 to about 600. Preferably, the content of residual monomeric hexamethylene diisocyanate in these products is below about 0.5 % by weight.

[0057] Preferred examples of catalysts for the preparation of polyurethane gels for use in the present invention are bismuth(III) carboxylates based on linear, branched, saturated or unsaturated carboxylic acids having about 2 to about 18 carbon atoms, preferably about 6 to about 18 carbon atoms, which carboxylates are soluble in the above anhydrous polyether polyols (a). Bi(III) salts of branched, saturated carboxylic acids with tertiary carboxyl groups, such as 2,2-dimethyloctanoic acid (for example, Versatic acids, Shell) are particularly preferred. Compositions of these Bi(III) salts in excess amounts of these carboxylic acids are frequently used. A solution of 1 mole of the Bi(III) salt of the Versatic 10 acid (2,2-dimethyloctanoic acid) in an excess of about 3 mole of this acid with a Bi content of about 17 % has proven outstanding.

[0058] It is preferred to use the catalysts in quantities of from about 0.03 to about 0.25 %, in particular, to about 0.1% by weight, based on the polyol component (a).

[0059] Non-limiting examples of antioxidants which may be contained in the polyurethane gels and other polyurethane resins for use in the present invention comprise, in particular, sterically hindered phenolic stabilizers, such as BHT (2,6-di-tert-butyl-4-methylphenol), Vulkanox BKF (2,2'-methylene-bis-(6-tert-butyl-4-methylphenol) (Bayer AG, Germany), Irganox 1010 (pentaerythrityl tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate]), Irganox 1076 (octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate) (Ciba-Geigy, Switzerland) and tocopherol (Vitamin E). The use of antioxidants of the α -tocopherol type is particularly preferred. The antioxidants are preferably used in amounts of from about 0.15 to about 0.5 % by weight based on the polyol component (a).

[0060] The isocyanate index (ratio of the free NCO groups and the free OH groups used in the reaction) of, e.g., polyurethane gel compositions suitable for use in the present invention generally is in the range of from about 0.30 to about 0.70, preferably in the range from about 0.45 to about 0.60, depending to some extent on the functionality of the polyisocyanate and polyol components employed. The isocyanate index necessary for gel formation can be estimated by using the following formula:

$$f_{(polyol)} \cdot (f_{(isocyanate)} - 1) \cdot index \approx 2$$

$$index \approx \frac{2}{f_{(polyol)} \cdot (f_{(isocyanate)} - 1)}$$

f: functionality of the polyisocyanate or polyol component

[0061] Depending on the desired tackiness or elasticity of the gel, the isocyanate index for affording optimum results may deviate from the calculated value by up to \pm about 20 %. The polyurethane gel compositions for use in accordance with the present invention may be prepared by conventional processes, as described, for example, in Becker/Braun, *Kunststoff-Handbuch*, Vol. 7, Polyurethane, p. 121 ff., Carl-Hauser, 1983.

[0062] Additional preferred examples of polyurethane gel compositions for use in the present invention are disclosed in EP 0 665 856 A. According to this document, polyurethane gel compositions are obtainable from

1. a polyurethane gel which comprises
 - (A) about 25-62 % by weight, preferably about 30-60 % by weight, particularly preferably about 40-57 % by weight, based on the total of (A) and (B) of a covalently cross-linked polyurethane as high molecular weight matrix and
 - (B) about 75-38 % by weight, preferably about 70-40 % by weight, particularly preferably about 60-43 % by weight, based on the total of (A) and (B), of one or more polyhydroxy compounds which are firmly bonded to the matrix by secondary valence forces and have an average molecular weight between about 1,000 and about 12,000, preferably between about 1,500 and about 8,000, particularly preferably between about 2,000 and about 6,000, and an average OH number between about 20 and about 112, preferably between about 25 and about 84, particularly preferably between about 28 and about 56, as liquid dispersant, the dispersant being essentially free of hydroxy compounds with a molecular weight below about 800, preferably below about 1,000, particularly preferably below about 1,500 and, optionally,

(C) 0 to 100 % by weight, based on the total of (A) and (B), of fillers and/or additives,

which gel composition is obtainable by reacting a mixture of

- (a) one or more polyisocyanates,
- (b) one or more polyhydroxy compounds with an average molecular weight between 1,000 and 12,000, and with an average OH number between 20 and 112,
- (c) optionally, catalysts or accelerators for the reaction between isocyanate groups and hydroxyl groups and, optionally,
- (d) fillers and additives,

this mixture being essentially free of hydroxyl compounds with a molecular weight below 800, the average functionality of the polyisocyanates (F_I) being between 2 and 4, the average functionality of the polyhydroxy compounds (F_P) being between 3 and 6, and the isocyanate index (K) being represented by the formula

$$K = \frac{300 \pm X}{(F_I \bullet F_P) - 1} + 7$$

in which $X \leq 120$, preferably $X \leq 100$, particularly preferably $X \leq 90$, and the index K has values between about 15 and about 70, where the stated averages of molecular weight and OH number are to be understood as number averages,

- 2. a water-absorbing material and/or
- 3. a non-aqueous foaming agent.

[0063] Where a self-adhesive polyurethane is to be produced, the conditions defined above should be adhered to in selecting the gel-forming components, since otherwise non-adhesive, elastic gels rather than self-adhesive gels may be obtained.

[0064] Preferred polyhydroxy compounds are polyether polyols, as are listed in detail in the above-mentioned applications.

[0065] Suitable as polyisocyanate components for use in the synthesis of the above polyurethane gels and other polyurethanes for use in the present invention are both (cyclo)aliphatic and aromatic polyisocyanates. Preferred (cyclo)aliphatic polyisocyanates

are 1,6-hexamethylene diisocyanate and its biurets and trimers, and hydrogenated diphenylmethane diisocyanate ("MDI") types. Preferred aromatic polyisocyanates are those obtained by distillation, such as mixtures of the 4,4'- and 2,4'-isomers of MDI, 4,4'-MDI, and toluylene diisocyanate ("TDI") types.

[0066] The polyisocyanates may be chosen, for example, from unmodified aromatic or aliphatic diisocyanates or else, from modified products thereof as formed by prepolymerization with amines, polyols, including polyether polyols and the like.

[0067] Polyurethanes have several properties which make their use in the present invention particularly advantageous:

- Polyurethanes can be prepared both as self-adhesive and non-adhesive polymers, as desired.
- When self-adhesive polyurethane systems are employed, the addition of adhesives that under certain circumstances may induce side effects such as maceration, inflammation of the dermal areas, reduced cutaneous respiration, etc. can be dispensed with.
- Self-adhesive polyurethanes are advantageous as compared to other adhesive materials, such as polyacrylates, rubber, etc., since they have no allergy potential.
- Polyurethanes have very good permeability to water vapor. As a result, the release of water through the skin does not cause maceration in the case of application for a relatively long time period.
- The oxygen permeability of polyurethanes ensures the necessary oxygen supply to the covered skin area, thus preventing damage to the tissue.
- Polyurethanes are hypoallergenic, so no allergic reactions will occur after application.
- In contrast to other materials such as many hydrocolloids and hydrogels, polyurethanes exhibit no tendency to disintegrate when in relatively long contact with fluids such as wound exudate. Consequently, a polyurethane wound dressing, for example, that is left in contact with wound fluids for a relatively long period, leaves no residues in the wound that hinder wound healing.
- Self-adhesive polyurethanes lose their adhesiveness on contact with liquid, thereby avoiding sticking to freshly formed tissue and, moreover, permitting painless removal of a corresponding wound covering.

- Polyurethane wound coverings in accordance with the present invention generate a moist wound environment, which leads to faster wound healing.

[0068] As mentioned above, the polyurethane material used in the present invention may be partially or fully foamed or substantially unfoamed. Foaming of the polyurethane material results in a softer matrix system, which provides a pleasant texture for the user and makes it possible to manufacture an article such as a dressing that conforms better to the body. Moreover, foamed wound coverings provide a cushioning effect, which may be desirable in pressure-sensitive applications such as burn injuries.

[0069] However, it may also be advantageous to use a polyurethane material which is substantially unfoamed. Such a material will still have excellent properties. According to the present invention, the release of the silver usually does not depend on the foam structure to any significant extent.

[0070] Fillers and other additives may be added to the polyurethane resin for use in the present invention. Non-limiting examples thereof are inorganic or organic short fibers, superabsorbers, pigments such as, e.g., titanium dioxide, zinc oxide and metal pigments, plasticizers, colorants, surface-active agents, and liquid extenders such as, e.g., substances with a boiling point above 150 °C, etc.

[0071] Examples of inorganic fillers include barite, calcium carbonate, gypsum, kieserite, soda, cerium dioxide, silica sand, kaolin, carbon black and microbeads.

[0072] Non-limiting examples of organic fillers that may be used include powders on the basis of polystyrene, polyvinyl chloride, urea formaldehyde resin and polyhydrazodicarbonamide.

[0073] Non-limiting examples of short fibers that may be used include, for example, glass fibers about 0.1 – 1 mm in length and fibers of organic origin, for example polyester or polyamide fibers.

[0074] Metal powders, such as iron, aluminum or copper powders, may be used as well.

[0075] The addition of a pigment such as, e.g., titanium dioxide, preferably in an amount of about 0.01 to about 2% by weight based on the polyurethane resin, improves the aesthetic appeal of the wound covering article of the present invention in that the user cannot see any unaesthetic blood through a dressing, for example.

[0076] Organic and inorganic colorants and/or pigments may be used according to the present invention to impart a desired color to the polyurethane resin composition. Non-limiting examples thereof are iron oxide and chromic oxide pigments, and phthalocyanine and monoazo based pigments.

[0077] Cellulose powder, activated charcoal and silicic acid may be mentioned as non-limiting examples of surface-active substances for use in the present invention..

[0078] The addition of coloring agents and the like to the polyurethane resin composition is not mandatory, since no discoloration of the silver glass containing polyurethane resin will take place. Rather, coloring with additional substances will usually serve to individualize the finished product, for example to make it more attractive for children or to adapt it to specific environmental parameters such as skin color.

[0079] A superabsorber (preferably in the form of a powder) may be used in the article of the present invention, e.g., for holding (particularly large amounts of) fluid. The superabsorber helps absorb the fluid that is released from the skin area, thus countering maceration and keeping the wound covering article from coming off prematurely. In addition, in the case of open wounds, the increased retention of secretions from the wound and the increased absorption of pathogenic microorganisms associated therewith affords a significant advantage.

[0080] Preferred water-absorbing materials for use as superabsorbers are water-absorbing salts of polyacrylates and copolymers thereof, in particular the sodium or potassium salts. These products are commercially available, and may be non-crosslinked or crosslinked. Particularly preferred products are products disclosed in DE 37 13 601 A1, and superabsorbers of the new generation with a low residual water content, which can be removed, and a high swelling capacity under pressure. Specific examples of these preferred products include polymers based on acrylic acid/sodium acrylate with a small amount of crosslinking. Sodium polyacrylates of this type can be obtained under the trade name Favor 22-SK (Stockhausen & Co. KG, Germany). Other superabsorbers are suitable as well, for example, carboxymethylcellulose and karaya.

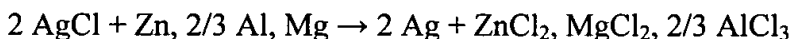
[0081] It is advantageous to incorporate the superabsorber or superabsorbing polymer in an amount of from about 0.01 % to about 40% by weight, particularly from about 0.5

% to about 30% by weight, more particularly about 20 % by weight, based on the weight of the polyurethane resin.

[0082] According to preferred embodiment of the present invention, elemental aluminum, zinc and/or magnesium and/or basic compounds thereof such as, e.g., zinc hydroxide or magnesium chloride, may be added to the polyurethane resin. The addition of these substances (preferably in anhydrous form) may, for example, take place during the synthesis of the polyurethane resin and/or the incorporation of the silver glass.

[0083] These substances may increase the quantity of the antimicrobial silver glass that can be combined with the polyurethane resin and/or they may permit the addition of further antimicrobial compounds, such as silver zeolites. Additionally, the addition of elemental aluminum, zinc and/or magnesium and/or the basic compounds thereof may prevent the undesirable black discoloration of the conventional silver compounds, if present.

[0084] Particularly, the moisture from the wound or from the environment causes a conversion of the silver to silver chloride or silver oxide, which can cause known silver containing wound covering materials to look unappealing and to lose efficacy. The addition of aluminum, zinc or magnesium allows regeneration of the antimicrobially active silver in accordance with the electrochemical potentials of the reactions:



[0085] In accordance with the present invention, the elemental Al, Zn, Mg and/or the basic compounds thereof, are preferably employed in a (total) amount of from about 0.01 to about 5% by weight, based on the weight of the polyurethane resin.

[0086] To modify the adhesion characteristics of a given polyurethane resin, vinyl polymers, polyacrylates and other polymers and copolymers which are suitable for use as adhesives, as well as adhesives based on natural substances, may be added to the polyurethane resin, usually in a concentration of up to about 10 % by weight, based on the weight of the polyurethane resin, without diluting or impairing the advantageous properties of the polyurethane resin.

[0087] The article of the present invention comprises a particulate glass which contains silver.

[0088] The term "antimicrobial" as used in the present specification and the appended claims is to be understood in its broadest sense, and is inclusive of terms like "disinfectant", "antibacterial", "antifungal" etc. In particular, "antimicrobial" denotes activity against pathogenic microorganisms of any kind.

[0089] In addition to Ag, the glass for use in the present invention will usually comprise at least P_2O_5 , one or more of CaO, MgO, ZnO and CuO; and one or more of Al_2O_3 , SiO_2 , and B_2O_3 as glass forming elements. Often it will also comprise one or more of Na_2O , K_2O and Li_2O , as well as one or more other elements which are frequently present in glass (e.g., metals, including transition metals and rare earth elements, for example, in order to change the color of the glass or the melting point thereof, etc.). However, if one or more other elements are present, the total amount thereof will usually not exceed about 5 mole-%, particularly not exceed about 2 mole-%, e.g., not exceed about 1 mole-%, calculated as oxides and based on the total glass composition. Preferably, the glass is substantially colorless and/or transparent. This is even more preferred in cases where the polyurethane resin is substantially colorless and/or transparent as well.

[0090] In this regard, it is to be understood that while the glass forming elements are represented herein in the form of their oxides, this is merely to follow the convention in the art, and should by no means construed to indicate that these elements must be present as oxides. Rather, the elements can be present in any form, e.g., as salts, complexes and the like. By the same token, the mole and weight percentages given herein are calculated based on the assumption that all of the indicated elements are present in the oxide form, even if in reality some of them are not. Again, this calculation corresponds to the convention in the glass field. Furthermore, unless indicated otherwise, all mole and weight percentages of the glass components given herein are based on the totality of all elements present in the glass, each element being represented and calculated as oxide.

[0091] P_2O_5 will often be a major component of the glass for use in the present invention. It will usually be present in an amount of at least about 30 mole-%, e.g., at least about 35 mole-%, at least about 40 mole-%, or even at least about 45 mole-%, and usually in an amount of not more than about 75 mole-%, e.g., not more than about 70 mole-%, not more than about 65 mole-%, not more than about 60 mole-%, not more than about 55 mole-%, or even not more than about 50 mole-%.

[0092] One or more of CaO, MgO, ZnO and CuO will usually be present in the glass for use in the present invention in a total amount of at least about 20 mole-%, e.g., at least about 25 mole-%, at least about 30 mole-%, or even at least about 35 mole-%, and usually in a total amount of not more than about 55 mole-%, e.g., not more than about 50 mole-%, or even not more than about 45 mole-%. Preferably, the glass for use in the present invention contains one or both of CaO and MgO, e.g., at least MgO alone.

[0093] One or more of Al₂O₃, SiO₂, and B₂O₃ will usually be present in the glass for use in the present invention in a total amount of at least about 5 mole-%, e.g., or even at least about 10 mole-%, and usually in a total amount of not more than about 50 mole-%, e.g., not more than about 40 mole-%, not more than about 30 mole-%, not more than about 20 mole-%, or even not more than about 15 mole-%. Preferably, the glass for use in the present invention contains both Al₂O₃ and SiO₂, or at least Al₂O₃ alone. Al₂O₃ will usually be present in an amount of at least about 5 mole-%, although usually not more than about 10 mole-%. The amounts of SiO₂, when present, can be as high as about 50 mole-%, particularly in cases where the content of P₂O₅ is at the lower end of the indicated range.

[0094] One or more of Na₂O, K₂O and Li₂O will often be present in the glass for use in the present invention in a total amount of not more about 5 mole-%, e.g., not more than about 3 mole-%, or even not more than about 2 mole-%. More frequently, the glass for use in the present invention may contain one or both of Na₂O and K₂O, or Na₂O alone.

[0095] The glass for use in the present invention will include Ag₂O in an amount of usually at least about 0.1 % by weight, e.g., at least about 0.2 % by weight, at least about 0.5 % by weight, at least about 0.8 % by weight, or even at least about 1 % by weight, although the content of Ag₂O will usually not exceed about 10 % by weight, e.g., not exceed about 8 % by weight, not exceed about 5 % by weight, not exceed about 3 % by weight, or even not exceed about 2.5 % by weight.

[0096] In this regard, a particularly preferred glass for use in the present invention has the following approximate composition:

	% by weight
P ₂ O ₅	about 73.5
MgO	about 18.5
Al ₂ O ₃	about 6.5
Ag ₂ O	about 2

[0097] Corresponding antimicrobial glasses are available from a variety of commercial sources, for example, Ishizuka Glass Co. Ltd., Japan, and Mo-Sci Corporation, U.S.A.

[0098] The article of the present invention will usually contain the glass which comprises silver in an amount, based on the total weight of this glass and the polyurethane resin (without fillers, additives etc.), of at least about 0.01 % by weight, e.g., at least about 0.05 % by weight, at least about 0.075 %, or at least about 0.01 % by weight. Usually, however, the amount of this glass will be not higher than about 40 % by weight, e.g., not higher than about 20 % by weight, not higher than about 10 % by weight, not higher than about 5 % by weight, not higher than about 2 % by weight, or not higher than about 1 % by weight. Of course, two or more different kinds of silver containing glass can be used in combination according to the present invention. By way of non-limiting example, two different kinds of silver containing glass may be used, e.g., a first glass which releases silver at a faster rate and/or releases silver in a higher or lower amount than a second glass used in combination therewith.

[0099] Preferably, the antimicrobial glass will have a residual moisture content of not more than about 5 % by weight, e.g., not more than about 2.5 % by weight.

[0100] Any desired shape of the particulate glass may be employed, e.g., (short) fibers, granules, (micro)beads, microspheres, flakes, etc. However, the particle size should be small enough to not significantly distract from the intended use of the article. Preferably, the volume-related particle size should not be higher than about 10 μm , e.g., not higher than about 5 μm , although no significant advantage may be obtained by decreasing the particle size to less than about 0.1 μm , or even less than about 1 μm . The glass may have been made by a variety of methods, for example, by casting (including centrifugal casting) and by rod, fiber and tube drawing. Other methods include glass foaming and comminution.

[0101] In general, the amount of the silver containing glass will be selected to provide an amount of Ag, expressed as mg Ag per kg of the composite which comprises the glass, the polyurethane resin and optionally employed additives, fillers etc, of at least about 5 mg/kg, e.g., at least about 10 mg/kg, at least about 20 mg/kg, or at least about 30 mg/kg, and usually not more about 200 mg/kg, e.g., not more about 150 mg/kg, not more about 100 mg/kg, or not more about 50 mg/kg.

[0102] Furthermore, it is preferred for the composite of the present invention to release the silver at a rate of at least about 5 mg, more preferably at least about 10 mg, per kg of composite, as determined by the method described below (i.e., over a period of 24 hours). Usually, the release rate will not be higher than about 100 mg/kg, e.g., not higher than about 50 mg/kg, or even not higher than about 30 mg/kg. The release rate can be controlled through the quantity and composition of the glass, and also, *inter alia*, through the choice and amount of optional additives.

[0103] The release of Ag ions from the article in accordance with the present invention (as determined by the test described below) will usually take place for a period of at least about 2 hours, e.g., at least about 10 hours, at least about 24 hours, at least about 96 hours, or even at least 240 hours, so that a long-term treatment of the wound is ensured. This obviates the need for a frequent changing of the article, e.g., a wound dressing.

[0104] The antimicrobial glass may be present in the article of the present invention in any form that permits at least a part of the glass to be associated with, preferably, be in direct contact with at least a part of the polyurethane resin. According to a preferred embodiment, the polyurethane resin forms a matrix in which the particulate glass is embedded. However, the glass may also be present in one or more different forms. Combinations of different forms of contact between glass and polymeric materials are possible as well. Of course, two or more different glasses may be used in combination with one or more polymeric materials.

[0105] The manner in which the glass and the polyurethane resin are combined with each other is apparently dependent, *inter alia*, on the desired structure of the composite. By way of non-limiting example, the polyurethane resin which may be present in molten form (e.g., in an extruder) or dissolved in a suitable solvent, and the particulate glass may be mixed and the resultant mixture may then be given the desired shape, optionally after

at least a part of the solvent has been removed. Alternatively, a solution or dispersion of the polyurethane resin in a solvent which also contains the particulate glass may be applied (by spraying, casting, extrusion, etc.) on a shaped body or layer formed by the same or a different polyurethane resin which may optionally already contain the same or a different particulate glass. Alternatively, the glass may be added before or during the reaction which affords the polyurethane resin.

[0106] For example, the particulate glass may be added to a reaction mixture comprising a polyol and a polyisocyanate, resulting in a highly homogeneous dispersion of the glass in the resulting polyurethane resin. It was found that the antimicrobial (e.g., silver containing) glass used in accordance with the present invention may be incorporated into a polyurethane matrix, by admixing the glass with the polymer starting materials, without interfering with the polymerization reaction. Of course, any other form of bringing the glass and the polymeric material into (permanent) contact with each other may be used as well.

[0107] It was found that the glass usually does not give rise to any significant degradation of the properties of the polyurethane matrix. Also, the glass usually will not be subject to discoloration (as a result of being exposed to, e.g., radiation and/or heat), even if the article is used for extended periods of time.

[0108] The article of the present invention may be employed in many different forms and shapes. A preferred article of the present invention has a sheet-like structure (foamed or not foamed), with a uniform or non-uniform thickness. The thickness of the sheet-like structure in this case will usually be at least about 100 μm , e.g., at least about 400 μm , or at least about 600 μm , but will usually be not higher than about 2,000 μm , e.g., not higher than about 1,500 μm , or not higher than about 1,200 μm .

[0109] Also, a sheet-like article of the present invention will usually have a water vapor permeability, determined according to the method described below, of at least about 100 $\text{g}/(\text{m}^2 \cdot 24\text{h})$, preferably at least about 250 $\text{g}/(\text{m}^2 \cdot 24\text{h})$, or even at least about 300 $\text{g}/(\text{m}^2 \cdot 24\text{h})$. On the other hand, the water vapor permeability will usually not exceed 5,000 $\text{g}/(\text{m}^2 \cdot 24\text{h})$, e.g., not exceed about 2,500 $\text{g}/(\text{m}^2 \cdot 24\text{h})$, or not exceed 1,500 $\text{g}/(\text{m}^2 \cdot 24\text{h})$.

[0110] The water absorption capacity of the polyurethane resin for use in the article of the present invention, determined by the method described below, usually will be at least about 0.5 g water per g of polyurethane resin, preferably at least about 1 g/g, or even at least about 1.5 g/g. It will usually be not higher than about 10 g/g, e.g., not higher than about 6 g/g, or not higher than about 3.5 g/g.

[0111] If the polyurethane resin for use in accordance with the present invention is made to be self-adhesive, additional means of affixing the article to the skin may be dispensed with. The article may be placed directly on the wound to be covered, e.g., as a bandaging material, and will adhere to the skin surrounding the wound due to its self-adhesive properties.

[0112] In the case of relatively large wounds and/or if additional adhesion is desired, or if the polyurethane resin is not made to be self-adhesive, the article may be adhered to the skin by the addition of an adhesive for the edge portion. A corresponding article in accordance with the present invention will have a structure similar to that of known products, e.g., known bandages. In this case, the article will generally comprise a backing material that is provided on one side with a self-adhesive coating. The article in accordance with the invention is then affixed to this self-adhesive coating. In order to ensure ease of use, the self-adhesive coating may further be covered with a protective layer, such as a sealing paper.

[0113] A non-limiting example of a suitable adhesive for use as the surface adhesive (= adhesive for the edge portion) which may be used in combination with the optional backing material is described in DE 27 43 979 C3. Alternatively and preferably, commercial pressure-sensitive acrylate-based or rubber-based adhesives may be used for the adhesive coating.

[0114] Particularly preferred surface adhesives are thermoplastic hot-melt adhesives based on natural and synthetic rubbers and other synthetic polymers such as acrylates, methacrylates, polyurethanes, polyolefins, polyvinyl derivatives, polyester or silicone, optionally with suitable additives such as tackifying resins, plasticizers, stabilizers, and other auxiliary materials as needed. In some cases, secondary cross-linking by UV or electron beam radiation may be of advantage.

[0115] Hot-melt adhesives based on block copolymers, in particular, are characterized by their wide versatility, since a controlled reduction of the glass transition temperature of the self-adhesive substance resulting from the choice of tackifier, plasticizers, molecule size and the molecular weight distribution of the starting components ensures the required bonding to the skin in a manner appropriate to their function, even at critical points of the human locomotor system.

[0116] A high shear strength of the hot-melt adhesive may be achieved through a high cohesiveness of the polymer. The good finger tack results from the range of tackifiers and plasticizers used. The adhesive composition preferably contains at least one aromatic component, which usually accounts for less than about 35 %, preferably from about 5 % to about 30 % by weight, of the adhesive. For systems which are to adhere particularly strongly, the hot-melt adhesive may preferably be based on block copolymers, especially A-B or A-B-A block copolymers or mixtures thereof. The hard phase A comprises primarily polystyrene or its derivatives and the soft phase B comprises ethylene, propylene, butylene, butadiene, isoprene or mixtures thereof, particular preference being given to ethylene and butylene or mixtures thereof. The controlled blending of diblock and triblock copolymers is particularly advantageous, with a diblock copolymer fraction of less than about 80% by weight being preferred.

[0117] In a preferred embodiment the hot-melt adhesive has the composition indicated below:

about 10 % b. w. to about 90 % b. w.	block copolymers,
about 5 % b. w. to about 80 % b. w.	tackifiers such as, e.g., oils, waxes,
	resins and/or mixtures thereof, preferably
	mixtures of resins
	and oils,
less than about 60 % b. w.	plasticizers,
less than about 15 % b. w.	additives,
less than about 5 % b. w.	stabilizers.

[0118] The aliphatic or aromatic oils, waxes and resins which are preferably used as tackifiers usually are hydrocarbon oils, waxes and resins, with the consistency of the oils, such as paraffinic hydrocarbon oils, or the waxes, such as paraffinic hydrocarbon waxes, being responsible for their favorable effect on bonding to the skin. The plasticizers will usually be selected from medium- or long-chain fatty acids and/or their esters. The plasticizers serve to adjust the adhesion properties and the stability. If desired, further stabilizers and other auxiliaries may be employed.

[0119] The carrier (backing) material for use in an article according to the present invention preferably comprises an air and water vapor permeable, but water-impermeable, polymeric layer. Usually, this layer will have a thickness of from about 10 μm to about 100 μm . The backing material, which under certain circumstances may be flexible, preferably comprises polymers selected from at least one of polyurethanes, polyethylene, polypropylene, polyamides, polyesters and polyether esters. However, other known backing materials such as, e.g., cloth, non-woven fabrics, foams, plastics, etc. may also be used.

[0120] The combination of polyurethane resin and glass may be affixed to the backing layer or film in a known manner. The resultant combination having the backing material on one side thereof may be applied to the skin as a composite sheet with the backing layer on top. The permeability to water vapor, the strength of the wound covering, the cushioning for pressure, as well as other physical properties of the wound covering may be controlled by the selection of the backing material.

[0121] When an article according to the present invention comes into contact with a wound exudate, it will usually absorb (at least a part of) the exudate, causing the polyurethane resin to swell. A particularly satisfactory absorption of wound exudate by when the polyurethane resin is used in combination with superabsorber materials.

[0122] Two important steps for wound healing can subsequently be identified. Firstly, silver ions are released by the (preferably finely distributed) glass in contact with the exudate, and secondly, pathogens from the wound can be taken up by the polyurethane resin. After application to an exuding wound, a silver glass containing article in accordance with the present invention will, through contact between the fluid and the silver glass, kill the pathogens in the wound fluid and/or prevent colonization of the

wound by microorganisms and possibly an infection. These two steps individually, and both of them synergistically, bring about a reduction in pathogen growth and/or the death of the pathogens. The antimicrobial article in accordance with the present invention thus will possess both bacteriostatic and bactericidal properties. When the article is removed, the antibacterial effect ceases. There is no need to wash the wound to remove, for example, previously applied antiseptics and antibiotics.

[0123] The invention described is thus based on the antimicrobial effect of antimicrobial silver containing glass in combination with a (preferably highly) absorbent polyurethane resin, which together achieve a synergistic effect. Moreover, a polyurethane wound covering in accordance with the present invention can have self-adhesive properties that allow it to be affixed to the intact skin on the edge of the patient's wound. Moreover, the present invention provides a new type of wound covering that can be used to treat infected wounds, or for preventive care against wound infections. The covering constitutes a barrier to microorganisms, preventing them from penetrating from outside, in that they are killed on contact with the antimicrobial wound covering.

[0124] The combination of a polyurethane resin such as, e.g., a hydroactive polyurethane resin with a silver containing glass results in advantageous product appeal for consumers in addition to great product stability. In particular, the unappealing dark discoloration exhibited by known silver containing materials, which may be unacceptable to the consumer, and which is caused in particular by moisture, light or γ rays, may be reduced significantly or even prevented entirely.

[0125] A particularly advantageous aspect of the present invention is that the antimicrobial glass can be incorporated without problems into a polyurethane matrix and thus makes it possible to prepare an antimicrobial wound dressing. Surprisingly, the content of antimicrobial glass in the polymer, the distribution thereof in the polymer, and also the concentrations of additives can be selected within wide ranges without sacrificing the advantages described herein.

[0126] Moreover, additional skin care and/or wound-healing ingredients that support regeneration of the skin can be incorporated into the polymer matrix. Non-limiting examples of active ingredients that may be added include vitamins such as, e.g., vitamin

E or vitamin C, essential oils, flavone and its derivatives, anti-inflammatory agents, analgesics, and combinations of two or more thereof.

[0127] The antimicrobial article in accordance with the present invention can thus be used in, for example, wound care as a wound covering that is self-adhesive or is provided with additional surface adhesive. Moreover, in addition to its use in wound healing, it may be used in other fields such as, e.g., in skin care, as skin protection, and for the prevention of skin damage.

BRIEF DESCRIPTION OF THE DRAWINGS

[0128] The present invention is further described in the detailed description which follows, in reference to the noted plurality of drawings by way of non-limiting examples of exemplary embodiments of the present invention, in which like reference numerals represent similar parts throughout the several views of the drawings, and wherein:

Figure 1 is a graph which shows the results of silver release tests carried out with samples of articles according to the present invention;

Figure 2 shows the results of discoloration tests carried out with samples of articles according to the present invention;

Figure 3 shows the result of discoloration test carried out with a sample of an article according to the present invention after sterilization with γ rays; and

Figure 4 shows the result of a discoloration test carried out with a sample of an article according to the present invention after an accelerated aging thereof.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

[0129] The particulars shown herein are by way of example and for purposes of illustrative discussion of the embodiments of the present invention only and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the present invention. In this regard, no attempt is made to show structural details of the present invention in more detail than is necessary for the fundamental understanding of the present invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the present invention may be embodied in practice.

[0130] Wound covering materials in accordance with the present invention are described below. Unless indicated otherwise, relative amounts and concentrations are based on the weight of the polyurethane resin.

[0131] The liquid absorption capacity and the water vapor permeability of the polyurethane resins for use in the present invention referred to above are determined according to the following methods:

Determination of liquid absorption capacity of polyurethane resin

[0132] A circular sample having a diameter of 2.2 cm is punched out and kept in an atmosphere of 23 +/- 2 °C and 50 +/- 5 % r.h. for one hour. Then, the sample is weighed and immersed as a whole in physiological saline of 23 +/- 0.5 °C for 3 hours. The sample is weighed again and the liquid absorption is calculated from the difference of weights before and after immersion.

Determination of water vapor permeability

[0133] The determination was carried out according to ASTM E 96 (water method), with following modifications:

The opening of the test flask was 804 mm².

The sample was kept for 24 h at 23 +/- 2 °C und 50 +/- 5 % r.h.

The distance between water level in the test flask and the sample was 35 +/- 5 mm.

After having been kept for 24 h at 37 +/-1.5 °C and 30 +/-3 % r.h., the test flasks containing the samples were weighed again.

Example 1

[0134] The following components 1 and 2 were prepared by mixing the ingredients for 24 hours on a roller block:

Component 1:

500.0 g	Polyether Polyol (Levagel, Bayer AG, Germany) ¹
1.9 g	Vitamin E (Tocopherol)
51.3 g	Isocyanate Prepolymer (Desmodur, Bayer AG) ²
144.4 g	Superabsorber (Favor T, Degussa Stockhausen, Germany) ³

1.3 g	TiO ₂
1.6 g	Silver containing glass (Ionpure B1, Ishizuka Glass Company, Japan) ⁴

Component 2:

30 g	Polyether Polyol (Levagel) ¹
3 g	Bi-Catalyst ⁵

¹ Pentaerythritol/propylene oxide/ethylene oxide copolymer capped by an ethyleneoxide block; functionality: 4; OH number: 35; average molecular weight (calculated): 6,400; viscosity (23°C): 1,000 mPas; content of ethylene oxide: 20 % by weight.

² NCO-terminate prepolymer prepared by reacting, at 80 °C, hexamethylene diisocyanate (HDI) and polypropylene glycol (average molecular weight: 220) in a molar ratio of 5:1 and subsequent vacuum distillation to a content of residual HDI monomer of < 0.5 % by weight; NCO content: 12.6 % by weight; viscosity (23 °C): 5,000 mPas.

³ Cross-linked sodium polyacrylate.

⁴ P₂O₅ 73.35 % by weight ; MgO 18.33 % by weight; Al₂O₃ 6.32 % by weight; Ag₂O 2 % by weight.

⁵ Solution of 1 mol of Bi(III) salt of 2,2-dimethyloctanoic acid in 3 mol of 2,2-dimethyl octanoic acid (Bi content about 17 % by weight; a corresponding product is commercially available under the trade name Coscat).

[0135] A total of 500 g of the above component 1 and 3 g of the above component 2 were mixed by hand for 40 seconds and the resultant mixture was poured onto release paper and spread thereon so as to obtain an area weight of the polyurethane composition of about 800 g/m². Curing was then carried out for 5 minutes at 65 °C.

[0136] Pieces of a predetermined size were punched out of the cured polyurethane composition on the release paper to form individual wound pads. These pads were placed on the acrylate adhesive coated side of a polyurethane sheet (water vapor permeability about 350 g/(m²*24h)) with the release paper facing away from the polyurethane sheet. The release paper was removed, the composite was covered with sealing paper and individual bandages were punched out such that the wound pads were uniformly surrounded by the acrylate coated PU sheet. The individual bandages were then sealed and sterilized (gamma radiation, 25 – 35 kGy).

Determination of release of silver

[0137] The release of silver was determined by extraction of silver from the wound dressing or the wound pad material (size: $9 \pm 1 \text{ cm}^2$) into a phosphate-buffered saline solution (30 ml of PBS-solution) at 31°C for a predetermined time (24 h). The PBS used for this method is described by Dulbecco (John Paul, 'Zell- und Gewebekulturen', Walter de Gruyter 1980, 92). The content of calcium and magnesium ions is adjusted to wound fluid levels (0.19 g/L of $\text{CaCl}_2 \times 2 \text{ H}_2\text{O}$; 0.27g/L of $\text{MgSO}_4 \times 7 \text{ H}_2\text{O}$ Geigy Scientific Tables, Vol. 3, Ciba-Geigy Ltd., 8. Ed. 1984, p. 82). Following the extraction, the sample is carefully removed and the amount of extracted silver in the aqueous phase is determined, after acidification of the sample, by atomic absorption spectroscopy at a wavelength of 328.1 nm in an air/ C_2H_2 flame.

[0138] A release of 20 – 25 mg of silver / m^2 of wound covering (over 24 h) was determined.

Example 2

[0139] A silver glass containing polymeric composite according to the present invention was produced from the following materials:

Polyether polyol (Levagel):	16.50 g
Cross-linking agent (Desmodur)	1.70 g
Vitamin E	0.10 g
Superabsorber (Favor T)	2.05 g
Silver glass (Ionpure B1)	0.10 g
Bi-Catalyst	0.04 g
Total	<hr/> 20.50 g

[0140] The release of Ag^+ ions from the resultant composite was determined by the following method;

[0141] A sample A (1 g) of the composite in the form of a sheet having an area weight of about 800 g/m^2 was placed in 100 ml of 0.9 % NaCl solution for a predetermined

period of time and the amount of silver extracted from the sample was determined by atomic absorption spectroscopy. The results are shown in Table 1 below.

[0142] Comparable samples of known materials with silver zeolites (B) or silver zirconium phosphates (C), for which an antimicrobial activity had previously been demonstrated, released the silver in quantities which are also listed in Table 1.

Table 1: Release of Ag

Time (h)	Quantity of Ag Released (mg/kg)		
	A	B	C
24	23.8	14.4	28.5
72	25.4	25.0	23.4
168	28.3	26.5	29.6

[0143] The results summarized in Table 1 show that the release of silver ions by the composite in accordance with the present invention (A) and by the known materials with silver zeolites (B) or silver zirconium phosphates (C) is of the same order of magnitude.

Example 3

[0144] Composites in accordance with the present invention having contents of silver glass different from that of the composite of Example 2 were produced from the following materials.

Sample D

Polyether polyol (Levagel):	14.505 g
Cross-linking agent (Desmodur)	1.391 g
Vitamin E	0.057 g
Superabsorber (Favor T)	4.524 g
Silver glass (Ionpure B1)	0.002 g
Bi-Catalyst	0.041 g
Total	<hr/> 20.520 g

Sample E

Polyether polyol (Levagel):	14.41 g
Cross-linking agent (Desmodur)	1.38 g
Vitamin E	0.06 g
Superabsorber (Favor T)	4.50 g
Silver glass (Ionpure B1)	0.01 g
Bi-Catalyst	0.04 g
Total	<hr/> 20.39 g

Sample F

Polyether polyol (Levagel):	14.41 g
Cross-linking agent (Desmodur)	1.38 g
Vitamin E	0.06 g
Superabsorber (Favor T)	4.51 g
Silver glass (Ionpure B1)	0.016 g
Bi-Catalyst	0.04 g
Total	<hr/> 20.41 g

Sample G

Polyether polyol (Levagel):	79.03 g
Cross-linking agent (Desmodur)	7.65 g
Vitamin E	0.30 g
Superabsorber (Favor T)	22.76 g
Silver glass (Ionpure B1)	0.11 g
Bi-Catalyst	0.36 g
Total	<hr/> 110.22 g

Sample H

Polyether polyol (Levagel):	78.68 g
Cross-linking agent (Desmodur)	7.57 g

Vitamin E	0.30 g
Superabsorber (Favor T)	22.66 g
Silver glass (Ionpure B1)	0.28 g
Bi-Catalyst	0.36 g
Total	<hr/> 109.86 g

Sample I

Polyether polyol (Levagel):	78.95 g
Cross-linking agent (Desmodur)	7.58 g
Vitamin E	0.31 g
Superabsorber (Favor T)	22.74 g
Silver glass (Ionpure)	0.57 g
Bi-Catalyst	0.36 g
Total	<hr/> 110.51 g

Sample J

Polyether polyol (Levagel):	79.16 g
Cross-linking agent (Desmodur)	7.55 g
Vitamin E	0.30 g
Superabsorber (Favor T)	22.91 g
Silver glass (Ionpure B1)	1.14 g
Bi-Catalyst	0.36 g
Total	<hr/> 111.42 g

Example 4

[0145] Samples D – J (area weight about 800 g/m²) from Example 3 were tested with regard to their silver ion release after 24 h using the following method.

[0146] A sample (30 cm²) was placed in 100 ml isotonic saline solution at 32 °C. After 24 h the sample was removed and the solution was filtered through a 0.45 µm membrane filter, whereafter the concentration of the silver in the solution was determined using graphite tube AAS. The table below and Figure 1 summarize the results.

Sample	% by weight of silver glass in sample	Release of Ag (mg Ag/kg sample)
D	0.01	1.6
E	0.05	5.2
F	0.075	9.4
G	0.1	13.0
H	0.25	20.0
I	0.52	22.0
J	1.02	20.0

Example 5

[0147] Samples G and I were tested for antimicrobial activity according to JIS 2801:2000 for

- Escherichia coli IFO 3972
- Staphylococcus aureus IFO 12732.

The antimicrobial activity of the samples was calculated according to equation (1) below:

$$\text{Antimicrobial activity} = \log_{10} \frac{\text{Number of living bacteria at beginning}}{\text{Number of living bacteria after 24 h}} \quad (1)$$

[0148] Antimicrobial activity may be assumed at a value of >2, which means that the number of tested bacteria was reduced by a factor of >100.

[0149] As shown in Table 2, all tested samples possess adequate antimicrobial activity.

Table 2: Antimicrobial Activity

Sample	Ag Release after 24 h [mg/mg]	Antimicrobial Activity per Equation (1)	
		Escherichia coli	Staphylococcus aureus
G	13	> 3.6	> 3.3
I	22	> 3.6	> 3.3

I sterile	20	> 3.6	> 3.3
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Example 6

[0150] To compare the stability against discoloration of the articles in accordance with the present invention, samples D through J from Example 3 were tested for their color change caused by the addition of the silver glass. Figure 2 shows samples D through J as a black and white copy. No change in color as compared to the undoped reference sample is visible up to sample H. Only at a concentration above 0.25 % by weight of silver glass (sample H) can a slight color change be discerned that is difficult to see with the naked eye.

Example 7

[0151] To test the stability of the silver glass during sterilization, sample J from Example 3 was γ -sterilized with 26 kGy. As can be seen from Figure 3, the γ -sterilization does not produce any color change. A γ -sterilization of the finished composite did not cause any loss in antimicrobial activity per JIS Z 2801:2000 and, surprisingly, also did not cause any discoloration of the composite.

Example 8

[0152] To test stability with regard to aging of the composites in accordance with the present invention, sample G from Example 3 above was subjected to accelerated aging for 6 months at 50 °C and evaluated with regard to color stability. Here, too, no color changes were observed, as can clearly be seen even from the b/w copies reproduced in Figure 4. This shows that the composite of the present invention shows high discoloration stability under regular and even more severe conditions. However, it is noted that under extremely harsh conditions, i.e., prolonged exposure to bright sunlight, a discoloration of composites according to the present invention has occasionally been observed.

[0153] It is noted that the foregoing examples have been provided merely for the purpose of explanation and are in no way to be construed as limiting of the present invention. While the present invention has been described with reference to an exemplary

embodiment, it is understood that the words which have been used herein are words of description and illustration, rather than words of limitation. Changes may be made, within the purview of the appended claims, as presently stated and as amended, without departing from the scope and spirit of the present invention in its aspects. Although the present invention has been described herein with reference to particular means, materials and embodiments, the present invention is not intended to be limited to the particulars disclosed herein; rather, the present invention extends to all functionally equivalent structures, methods and uses, such as are within the scope of the appended claims.